AMENDMENT TO THE SPECIFICATION

Please amend the sequence listing by entering the substitute sequence listing filed herewith.

Please amend the Table at page 16, line 13 as follows:

Mutation	Probe Sequence	Hybridisation Temperature
M1 (D187H)	GGGTGTTCAAGGTCTCA (SEQ. ID. NO. 11)	55°C
M2 (V103L)	GTCAGCAGCAATGGGTGCTC (SEQ. ID. NO. 12)	55°C
M3 (P98L)	TGCTCCTCCAGGGCCAC (SEQ. ID. NO. 13)	65°C
M4 (T162M)	GATGGGCACCATGTGGGT (SEQ. ID. NO. 14)	65°C

Please amend the paragraph beginning at page 33, line 26 as follows:

Partial sequencing of γ-actin cDNA was performed in CCRF/CEM, CEM/VCR R, CEM/VLB100, and the CEM/dEpoB 4X cells using primers G-Act 1F : ATGGAAGAAGAGATCGCCGC (SEQ. ID. NO.15) and G- Act 654R: TCGGCCGTGGTGGTGAA (SEQ. ID. NO.16). cDNA was amplified in 1X amplification buffer, 0.75mM dNTPs, 62ηg G-Act 1F, 62ηg G- Act 654R, pfu-turbo polymerase in a total reaction volume of 20μ1, using the following PCR cycling: 96°C lmin, 35 X (96°C lmin, 64°C lmin, 72°C 45sec), 72°C 10min. Amplified cDNA was purified using the QIA Filter Gel Extraction Kit (Quiagen, Hilden, Germany) and sequenced using fluorescence based cycle sequencing with BigDye terminators (PE Biosystems, Foster City, CA). Sequences were analysed by the Automated Sequencing Facility, Biological Sciences, University of NSW. The yactin sequence of the resistant cell lines was compared with that of the parental CEM cell line and the published sequence.

Please amend the paragraph beginning on page 36, line 35 as follows:

The expression levels of the three major actin spots were measured (data not shown). β- and γ-actin in CEM and VCR R cells are expressed at very similar levels. The same isoelectric forms of β- and γ-actin in VLB100 cells show a 1.7 and 2.0 fold

decrease in expression respectively, compared to CCRF-CEM. Although VLB100 cells express an extra isoform, γ'-actin, the total actin expression is ~~in~~ not significantly changed compared to the CEM or VCR R cells.

Please amend the paragraph beginning at page 37, line 23 as follows:

The approximate pI for the β-actin spot is 5.29, for the"normal" γ-actin is 5.31, and for the spot 19 found only in the VLB100 cells is 5.46. To determine the cause of the isoelectric shift seen for spot 19, MS/MS was performed on peptides showing different masses between the γ- and γ'-actin. Two peptide mass differences were seen by MALDI-TOF MS: peptides at 1968.1Da and 998.5Da in γ-actin; peptides at 1020.6 and 1954.1Da in γ'-actin (data not shown). The amino acid sequence of these peptides shows that peptide 998.5Da, DLT***D***YLMK (SEQ. ID. NO. 17), from spot 16VLB100 γ-actin matches to the published γ-actin sequence aal84 to 191, whilst the 1020.6Da peptide from VLB100 γ'-actin (spot19), DLT***H***YLMK (SEQ. ID. NO. 9), was the same peptide with a mutation of $D_{187} \rightarrow H_{187}$. Similarly, peptide 1954.1Da from γ'-actin (spot 19), VAPEEHP***V***LLTEAPLNPK (SEQ. ID. NO. 10), matched the published sequence between residues 96 to 113, and 1968.1Da from spot 16, VAPEEHP***L/I***LLTEAPLNPK (SEQ. ID. NO. 18 for leucine; SEQ. ID. NO. 19 for isoleucine) was found to be the same peptide but with a mutation of $V_{103} \rightarrow L_{103}$. As leucine and isoleucine differ by 0. 01Da mass, these two amino acids cannot be distinguished using MS/MS. Sequencing of the 998.5Da and 1954. 1Da peptides in CEM and VCR R revealed no changes from the published sequence. Confirmation of these mutations was obtained by cDMA sequencing (data not shown). cDMA sequencing of γ-actin from these cell lines detected heterozygous mutations G → C ($D_{187} \rightarrow H_{187}$), and G → T ($V_{103} \rightarrow L_{103}$). A silent mutation of G → A was also identified in VLB100 cells. No differences were found in the CEM and VCRR cells to that of the published sequence. Thus γ'-actin (spot 19) harbours a substitution of aspartic acid, a positively charged amino acid, for histidine, a neutral amino acid, resulting in a more basic isoelectric point and hence the basic charge shift seen by 2D-PAGE. The substitution of a valine to a leucine does not change the charge on the protein and thus VLB100 γ-actin (spot 16) migrates to the same position as the wild type γ-actin in CEM and VCRR cells.